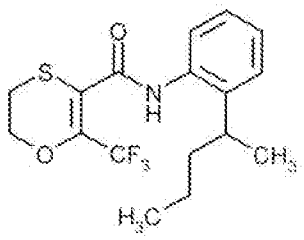
REMARKS

Applicants have amended Claims 19 and 20 to exclude halogens from the definition of group G^1.

Applicants acknowledge that examination has been restricted to only the elected species represented by the compound of Example 39 having the formula



and that Claim 33 has been withdrawn as not being drawn to the elected species. Claim 33 was also amended to reflect the same change to exclude halogen from the definition of group G^1. Applicants submit for the reasons discussed below that the elected species is allowable and that examination should be expanded to include the full scope of the claims. To this end, Applicants also present additional comparison data in new Declarations under 37 C.F.R. 1.132.

Rejections under 35 U.S.C. 103

A. Hahn et al article

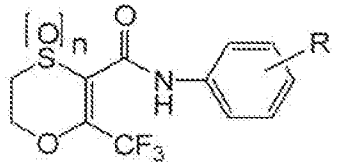
Claims 19-22, 28, and 33 stand rejected under 35 U.S.C. 103(a) as being unpatentable over the Korean language paper by Hahn et al, *Han'guk Nonghwa Kakhoechi* (translated as *J. Korean Soc. Agric. Chem. Biotechol.*), 44 (3), 191-196 (2001). Applicants again point out that the English translation of the Hahn et al paper that was kindly provided by the Examiner refers to antibacterial activity, whereas the English abstract attached to the original paper refers to antifungal activity. Based on a review of context, Applicants will again use the terms "fungicide" or "fungicidal" when referring to or citing the Hahn et al paper. Applicants respectfully traverse.

Applicants note at the outset that Claim 33 remains in this rejection despite being withdrawn. Applicants respectfully request joinder of Claim 33 upon finding their claims allowable.

The Office Action addresses Applicants' previous arguments as being based on differences in structure and on the sufficiency of their data. Applicants' response will address these points in the same order as summarized by in the Office Action.

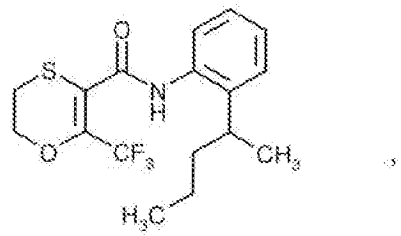
(1) Structural differences

Applicants again submit that structural features distinguish their claimed compounds from the compounds disclosed in the Hahn et al paper. As has been fully discussed in Applicants' previous Amendments, the reference in Table 1 discloses a very limited number and variety of specific dihydro-1,4-oxathiin carboxanilides having the formula



in which n is 0, 1, or 2 and R is hydrogen or one or two of a set of narrowly defined substituents that include methyl, trifluoromethyl, ethyl, isopropyl, methoxy, isopropyloxy, methylthio, fluoro, chloro, bromo, nitro, and cyano. Group R of the reference is thus clearly limited to relatively simple groups. [Applicants also note by way of comment with respect to expansion of examination that none of these substituents is related to Applicants' Z^2 (i.e., cycloalkyl or bicycloalkyl) or Z^4 (i.e., alkenyl or alkynyl).] Test data for some of these compounds are found in Table 2.

Applicants first note that substituent Z of their claimed compounds must always be attached through a carbon-to-carbon bond to the ortho position of the benzene ring. Applicants' elected species, the compound of Example 39 having the formula



exemplifies these requirements. Although the Hahn et al paper does disclose a few ortho-substituted substituents, the reference discloses only eight compounds in which an alkyl group is attached at an ortho position, namely compounds 17 (where R is 2-CF_3), 27 (where R is 2,5-dimethyl), 28 (where R is 2,4-dimethyl), 32 (where R is 2,6-diethyl), 34 (where R is 2,4,6-trimethyl), 38 (where R is 2-methyl), 52 (where R is 2-ethyl), and 53 (where R is 2-$CH(CH_3)_2$). See Table 1 (original at pages 194-195 and translation at pages 14 and 15). As already noted above, none of these compounds has an alkyl group having five or more carbon atoms as specified by Applicants for the unsubstituted C_5-C_{20}-alkyl members of their group Z^3 and none of

these compounds is a chlorine- or cycloalkyl-substituted alkyl as specified by Applicants for the substituted C_1-C_{20}-alkyl members of their group Z^3. Nothing in the reference suggests compounds other than those specifically disclosed.

Furthermore, based on the test results reported in the Hahn et al paper for compounds 21 and 40 (where R is respectively 3-isopropoxy and 3-isopropyl, both of which are thus at the meta position) relative to the other compounds disclosed in the reference and based on the known excellent fungicidal activity of "flutoranil" (more generally known as flutolanil, which also has a meta-isopropoxy phenyl moiety), the authors of the Hahn et al paper concluded that "the isopropoxy group or isopropyl group at the meta location of its phenyl group plays an important role" in fungicidal activity of such compounds. See translation at pages 15-16 (emphasis added). In view of the clearly stated preference for meta-substitution of the benzene ring with a three-carbon isopropoxy or isopropyl group, Applicants submit that the Hahn et al paper would not lead those skilled in the art to expect enhanced activity for other types of groups located at an ortho position, a specified requirement for the Y group of Applicants' invention (or, for that matter, located at a para position).

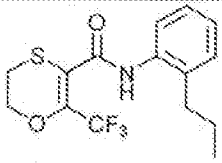
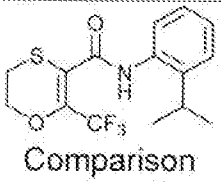
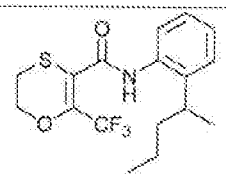
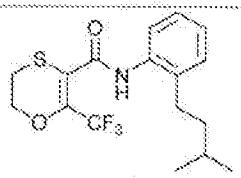
Applicants therefore again submit that these structural features are sufficiently different that those skilled in the art would not be led to their claimed invention.

The Office Action, however, asserts at page 3 that Applicants' elected species (and by extension their other claimed compounds) is merely a homolog of the known compound 53 and would thus be expected to exhibit similar activity. Even if the compounds might both be expected to exhibit fungicidal activity, Applicants submit that those skilled in the art would not be led to expect the enhanced activities found for the tested compounds of their claimed invention.

(2) Sufficiency of data

Notwithstanding the structural differences discussed above, the Office Action challenges the sufficiency of the data presented in the Declarations under 37 C.F.R. 1.132 of Dr. Ulrike Wachendorff-Neumann and Dr. Arnd Voerste because of supposed inconsistent results for comparison compound 53 of the reference and the absence of an error analysis of the data. Applicants respectfully submit that their data are not inconsistent or otherwise deficient.

By way of reminder, Applicants again provide a summary of the test results in the following table, which shows the structures of the tested compounds, the organisms and application rates used in the tests, and the observed test results.

Test	Efficacy (%)			
	 Comparison Cmpd [1]	 Comparison Cmpd 53 (Hahn et al)	 Inventive Cmpd 39	 Inventive Cmpd 102
Sphaerotheca (cucumber) 100 ppm (W-N D1) [2]	–	10	–	98
Venturia (apple) 100 ppm (W-N D1) [2]	–	57	–	100
Uromyces (bean) 100 ppm (W-N D2) [3]	–	10	95	–
Alternaria (tomato) 500 ppm (Voerste) [4]	0	0	95	–
Sphaerotheca (cucumber) 500 ppm (Voerste) [4]	0	0	94	–

[1] Comparison compound (similar to but not identical to Hahn et al)
[2] W-N D1 – From first Wachendorff-Neumann Declaration
[3] W-N D2 – From second Wachendorff-Neumann Declaration
[4] Voerste – From Voerste Declaration

More specifically with respect to the data for comparison compound 53, the Office Action at pages 3-4 continues to state that Applicants' data are unreliable because the *Sphaerotheca* tests reported in two of the Declarations produced different results for comparison compound 53 of the Hahn et al paper, thereby "suggest[ing] a statistical problem in the measurements." Applicants have fully explained the single perceived anomaly in the test results, which they assume is based on the slightly greater activity observed for comparison compound 53 when tested at 100 ppm (see first Wachendorff-Neumann Declaration) compared to the same compound tested at 500 ppm (see Voerste Declaration).

Applicants, although they cannot be absolutely certain of causation, again point out that the experiments were not carried out on the same days or in the same laboratories or even under identical conditions. One set of *Sphaerotheca* tests was carried out under the supervision and direction of Dr. Ulrike Wachendorff-Neumann using a mixture of equal parts acetone and dimethylacetamide as solvent (see Dr. Wachendorff-Neumann's first Declaration at page 2), whereas the other set of *Sphaerotheca* tests was separately carried out under the supervision and direction of Dr. Arnd Voerste using only dimethylacetamide as solvent (see Dr. Voerste's Declaration at page 2). Applicants maintain that those skilled in the art would understand that there could be some variation in test results.

However, even if one assumes – solely for the sake of discussion – that *Sphaerotheca* tests do produce some variability, for example, by as much as 10% (or 20% or even more), the relative differences in efficacies between comparison compound 53 and the inventive compound 39 (as in Dr. Voerste's Declaration) or inventive compound 102 (as in Dr. Wachendorff-Neumann's first Declaration) are so great, even with some variability, that those skilled in the art would conclude that the inventive compounds exhibit surprisingly and unexpectedly enhanced efficacies compared to the comparison compound. Applicants again refer to the established principal that "when an applicant demonstrates substantially improved results . . . and states that the results were unexpected, this should suffice to establish unexpected results in the absence of evidence to the contrary." *In re Soni*, 54 F.3d 746, 751, 34 U.S.P.Q.2d 1684, 1688 (Fed. Cir. 1995) (emphasis added). In view of the absence of any such contrary objective evidence, coupled with the strong differences in the test results discussed above and with the consistently high efficacies found in the other comparison experiments described in the three Declarations, Applicants submit that even without a strict statistical analysis, those skilled in the art would conclude that the compounds of their claimed invention are patentably distinct from the compounds taught by the reference.

Applicants maintain that the Office Action has not only been overly zealous in discounting the *Sphaerotheca* test data discussed above but has also improperly ignored the very strong data from the other tests, including data from the *Uromyces* test (see Dr. Wachendorff-Neumann's second Declaration) and from the *Alternaria* test (see Dr. Voerste's Declaration) that compare Applicants' elected species (i.e., the compound of their Example 39) with comparison compound 53 of the reference.

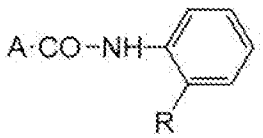
The data in these Declarations represent the results from four different tests carried out against four different organisms using two different application rates. In every single test, Applicants' inventive compounds always exhibited very high efficacy, whereas the comparison compounds did not. Even in the *Venturia* test, which gave the "closest" results, the differences in efficacy are dramatic. That is, regardless of the organism and the application rate and despite only modest structural differences for each tested pair of compounds, Applicants' inventive compounds always exhibited dramatically greater efficacies than the respective comparison compounds. In view of these consistently greater efficacies, Applicants submit that even without a strict statistical analysis, those skilled in the art would conclude that the compounds of their claimed invention are patentably distinct from the compounds taught by the Hahn et al paper. Applicants maintain that the Office Action provides no objectively based reason to doubt their showings of enhanced activities.

Applicants therefore again respectfully submit that their claimed invention is not rendered obvious by the Hahn et al paper.

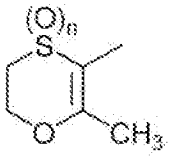
B. Eicken et al in view of Thornber article

Claims 19-22, and 28 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 5,589,493 ("Eicken et al") in view of the cited article by Thornber, *Chem. Soc. Rev.*, 8, 563-580 (1979). Applicants respectfully traverse.

Eicken et al discloses nicotinic anilide derivative of the formula



in which **R** is any of a host of substituents, including optionally substituted alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, alkynyloxy, cycloalkyl, cycloalkenyl, cycloalkyl-oxy, phenyl, or halogen, and **A** is optionally substituted pyridin-3-yl or phenyl of any of a number of heteroaromatic groups, one of which can have the formula (A2)



(A2)

(where n is 0, 1, or 2), used to combat Botrytis. E.g., column 1, lines 8-49, taken with column 17, line 15.

Eicken et al teaches that heteroaromatic group (A2) must always be only methyl-substituted and never bears a trifluoromethyl, difluoromethyl, or cyclopropyl

substituent as specified by Applicants. However, the Office Action in the paragraph bridging at pages 7 and 8 relies on the Thornber article as teaching at page 564 "how 'classical' isosteric replacement includes modifying a methyl group to a halogen" and accordingly refers to compounds 8.8 and 8.69 of the Thornber article (where R^7 is sec-pentyl and n is 2 and 1, respectively) as being of interest. Regardless of whether the Thornber article teaches that methyl can be replaced by a halogen (which could in any event be the case only for compounds of Applicants' invention in which group G^1 is a halogen), Applicants have amended their claims to exclude embodiments in which G^1 is halogen and present data in the form of additional Declarations showing unexpectedly enhanced properties for compounds in which G^1 is trifluoromethyl.

In particular, Applicants submit a third Declaration under 37 C.F.R. 1.132 of Dr. Ulrike Wachendorff-Neumann and a first under 37 C.F.R. 1.132 of Dr. Peter Dahmen showing the superiority of three compounds of their invention in which the G^1 substituent on the oxathiine ring is trifluoromethyl when compared with compounds within the scope of Eicken et al in which the corresponding substituent on the oxathiine group (A2) is necessarily methyl. More specifically, three sets of experiments were carried out using three pairs of compounds against three different fungi. Despite having alkyl side chains on the phenyl moiety that differ in number of carbon atoms and branching patterns (but otherwise within the scope of Applicants' group Z^3), Applicants' inventive trifluoromethyl-substituted compounds were always much more effective against the fungi than the corresponding comparative methyl-substituted compounds.

Applicants therefore submit that those skilled in the art would conclude that the compounds of their claimed invention are patentably distinct from the compounds taught by Eicken et al, whether taken alone or with the Thornber article.

Double Patenting Rejection

Claims 19-22, and 28 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-3 of copending Application No. 10/588,491. Applicants note that this application has published as Publication US 2008/0058389. Applicants respectfully traverse. Applicants, although they make no concession about obviousness, will offer an appropriate terminal disclaimer if their claims are otherwise found allowable.

In view of the preceding amendments and remarks, allowance of the claims is respectfully requested.

Respectfully submitted,

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Q:patents/prosecution documents/cs8582/8582 amendment 10-16-09